Marked-Up Version To Show Changes

IN THE SPECIFICATION

Amendment to page 1, lines 5-10

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of International Application PCT/US00/02051 filed on January 25, 2000 which is a CIP of U.S. Patent Application No. 09/236,758 filed on January 25, 1999, now abandoned, the entirety of each being specifically incorporated herein in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

The United States Government has certain rights in the present invention pursuant to Grant DE-AC05-96OR22464 from the United States Department of Energy.

Amendment to page 2, lines 27 and 30

One type of devices, often referred to as a "biochip" combines semiconductor detection system with biotechnology-based probes, and has received increasing interest. The inventor has developed a variety of self-contained biochip devices and systems (*e.g.,* U. S. Pat. Appl. Ser. No. 08/979,672, filed Nov. 26, 1997; Intl. Pat. Appl. Ser. No. PCT/US98/25294, filed Nov. 25, 1998, and U. S. Pat. Appl. Ser. No. 09/236,758, filed Jan. 25, 1999, the entire contents of each of which is incorporated herein by reference in its entirety). While such biochips (as well as other currently available biochip devices) have several detection channels, they are, however, designed to use only one specific type of bioreceptor at a time, and are therefore unsuitable for simultaneous multidetection of a plurality of [diverse biotargets] species. While these earlier biochip systems may be used for detecting either an individual or a plurality of a particular biochemical species on a single chip at the same time (*e.g.,* in detecting one or more polynucleotides or in detecting one or more polypeptides, they were not devised to detect

multiple [diverse] biochemical species at the same time on the same chip (*i.e.* the simultaneous detection of polypeptides and polynucleotides on a single chip).

Amendment to page 3, line 18

There is a critical demand for a rapid, simple, cost-effective technique for screening samples, such as blood or other clinical samples, for the presence of biomolecules (including polynucleotides, polypeptides, *etc.*) to assist in the diagnosis and treatment of medical diseases, including those caused by infectious pathogens, and the like, as well as provide efficient means for quantitating such molecules in pathology and forensics samples. The development of inexpensive screening analyses that would permit simultaneous analyses of multiple [diverse biotargets] biological molecules would allow rapid detection and improved treatments of many illnesses, facilitate improvements in quality control and manufacturing, as well as provide rapid, affordable devices for detection of biomolecules in the areas of environmental contamination and remediation processes.

Amendments to page 4, lines 22 and 27

There is also a distinct need for development of advanced multifunctional devices that permit the rapid, large-scale and cost effective analysis of pluralities of heterogeneous macromolecules, and permit the development of methods for detecting and quantitating multiple [diverse biotargets] molecular species in mixed biological samples.

2.0 SUMMARY OF THE INVENTION

This present invention overcomes these and other limitations in the prior art by providing for the first time, an advanced multifunctional biochip (AMB) that is capable of simultaneous detection of two or more [diverse macromolecule biotargets] different biological macromolecules (or "targets"). These macromolecules may comprise a plurality of polynucleotides (including DNAs, PNAs and/or RNAs), a plurality of polypeptides, peptides, and/or proteins; a plurality of enzymes, antibodies, and/or receptors or antigens); a plurality of pathogens, organisms, microorganisms, and/or viruses, *etc.*); or a plurality of cells, cell types, tissues, organelles, organs, fluids, and/or other intracellular or extracellular components of a living cell. Alternatively, the biological macromolecules may be a combination of any of these

or other biological compounds that may be detected using an AMB that comprises a plurality of receptor probes, or biomimetic probes on a single device. Such design permits the simultaneous or sequential detection of a variety of targets using a single biochip device, and as such provides methods of detecting and quantitating a number of diverse biochemical compounds using a single device.

Amendments to page 13, line 22:

4.0 DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

4.1 SOME ADVANTAGES OF THE INVENTION

The advanced multifunctional biochip system of the present invention offers a unique combination of performance capabilities and analytical features of merit not available in any other analysis system currently available. With its multichannel and multifunctional capabilities, the advanced biochip technology is the only current system that allows simultaneous detection of multiple [diverse] biomolecular targets simultaneously. The AMB devices of the present invention find utility in a wide variety of applications, and particularly in the areas of medical diagnostics, gene identification, and mapping, polynucleotide sequencing, environmental bioremediation, and related biotechnology applications.

Amendments to page 71, line 21:

Hybridization occurs between complementary DNA sequences and binding antibody-antigen was demonstrated by the fluorescence signals detected by the biochip. FIG. 4 shows that only fluorescence signals were detected on the biochip channels where hybridization of labeled DNA HIV1 (TB) gene probes with complementary bound-DNA fragments had occurred. This figure shows the simultaneous detection of HIV, TB and Goat IgG protein using HIV DNA probe (4 channels corresponding to the first row of the biochip), TB DNA probe (second row), and antibody probe for Goat IgG (fourth row). The blank signals (which correspond to DNA that is not complementary to the probes, or antigens not targeted by the antibody probes) are shown in the third row for comparison. The results demonstrate the use of the multifunctional biochip to detect more than one [diverse biotarget] type of macromolecule on a single chip device.